



Clinical Pharmacy Response to Evidence Report: Risk of Therapeutic Failure Due to Ineffectiveness of Medication



Tina Bayuse, Pharm.D., R.Ph.
Lead Pharmacist,
Johnson Space Center Pharmacy
Wyle/NASA

September 30, 2013

Bayuse

General Review

- How well the report:
 - Explains the current state of knowledge about the risk;
 - Summarizes the critical areas of debate about the risk;
 - Identifies the main gaps in knowledge or fundamental research about the risk; and
 - Addresses possible interactions between the risk of unpredicted medication effects and other risks identified in NASA's evidence reports

General Review

- Current report public August 2011
 - Update to report in review cycle; publish date unknown
 - Captures essence of the risk
 - Assumptions are terrestrial practice = microgravity practice
 - Report lists seven systems that could be impacted by the risk
 - Other evidence report reviews that involve medication are compounded by the unknown aspects of this risk
 - Bone, DCS, renal stone, reduced muscle mass (IM injection)

General Review

- Two major concerns highlighted
 - Pharmacokinetics/Pharmacodynamics (PK/PD)
 - The absence of evidence doesn't mean there is no risk
 - Extremely limited concrete information available
 - The use of medications without data to support their actual activities is a risk to the crewmember and the mission
 - Microgravity 'patients' are a specialized population due to the systemic changes that are known to occur
 - » additional changes/issues should be expected

General Review

- Two major concerns highlighted
 - Stability of Medications
 - Answers to the questions regarding the stability of the medications are not complete
 - Do shelf-life rules apply?
 - Need solid data to support extension for future missions
 - Information would help drive contents of medical kits

Clinical Pharmacy Perspective

- Question: Are there any operationally-relevant issues which have occurred over the years you worked for NASA?
- Question: Are there any issues you have raised which have NOT been addressed effectively?
 - Evidence report and the information therein are relevant to operations and in my opinion have not been addressed effectively
 - Stability of Medications
 - Medication expiration date consistently questioned
 - Resupply upmass, time, trash
 - Reality of pharmacy operations
 - » Pharmacy regulations come into play
 - » Market changes
 - Medical kit design and selection of medication

Clinical Pharmacy Perspective

- Question: Are there any operationally-relevant issues which have occurred over the years you worked for NASA?
- Question: Are there any issues you have raised which have NOT been addressed effectively?
 - Confounding elements – is the drug ‘bad’ or is there a PK/PD issue?
 - ‘Bad’ could mean expired, altered or both to the point of ineffectiveness
 - Clinical and operational issues blend
 - Changes to body systems
 - Medications used to treat symptoms
 - Medications used to handle occupational hazards
 - Polypharmacy at play
 - Environmental/engineering constraints

Clinical Pharmacy Perspective

- Question: Are there any operationally-relevant issues which have occurred over the years you worked for NASA?
- Question: Are there any issues you have raised which have NOT been addressed effectively?
 - Documentation of medication usage information
 - Processes evolving to get better information
 - Expect gaps due to crewmember's desire

Clinical Pharmacy Perspective

- We don't know the extent to which spaceflight alters pharmacodynamics
 - Actively discussed 'to do' or 'not to do' research
 - Anecdotally there is no clinically significant alteration
 - What about the asymptomatic clinically significant alteration?
 - Clinical Pharmacy: 'to do' review and research
 - The issue needs to be studied
 - New clinical issues have developed during the ISS missions
 - Is medication use a factor in new clinical issues? If so, what is the cause?
 - Exploration missions
 - Reasonable to expect additional concerns/issues

Clinical Pharmacy Perspective

- Insights regarding drug stability (pre, during and post-flight)
 - Pre-flight is the terrestrial model
 - Pharmacy Ops works hard to keep tabs on appropriate storage until spaceflight
 - Temperature data captured during shipment
 - During flight
 - Current medical kits are stored in their manufacturer's packaging wherever possible
 - Repackaging is kept to a minimum
 - Research report pending on 6 medications returned from spaceflight
 - Post-flight
 - Medications not returned routinely

Clinical Pharmacy Perspective

- Insights regarding drug stability (pre, during and post-flight)
 - Forward work
 - Integrated team looking at long-term and exploration flight concerns
 - Work being conducted through ExMC

Clinical Pharmacy Perspective

- Have any mitigation strategies regarding drug stability of particular dosage forms been altered as a consequence of the work Dr. Putcha's lab has been involved in (and published in the last 10 years?) Please provide specifics.
 - Mitigation strategies to date have been to select medications that have not been shown to be altered
 - Change in how most medications are packed (now using manufacturer's packaging wherever possible)
 - Ongoing research by the Pharmacology Lab

Clinical Pharmacy Perspective

- Are you aware of any specific drug misadventures which occurred as a consequence of likely altered PK/PD of a medication during spaceflight? Please provide specifics.
 - I am not aware of any specific drug misadventures that have occurred as a consequence of likely altered PK/PD
 - A systematic review has not been done to date
 - Processes are under development to use an integrated approach to medication use evaluation with a multi-disciplinary team

Clinical Pharmacy Perspective

- In your professional opinion, what should the research priorities be with regards to PK/PD and spaceflight?
 - Start with a baseline
 - Based on the clinical medication use evaluation, direction for PK/PD research is an expected outcome
 - In-flight research is necessary
 - One year mission
 - Needs to happen while on station and continue through to the next generation of missions

Clinical Pharmacy Perspective

- Evidence Report Review Summary
 - Current report captures the knowledge gap that exists with respect to the risk of therapeutic failure due to ineffectiveness of medication
 - Active research requests being made – hopefully translates to funding
 - The use of medications will continue to occur as we transition into exploration missions
 - Need to understand the impacts of the environment on medications and the interactions between pharmacologic therapy and the microgravity population to better inform clinical care